EXPRESS MAIL LABEL NO.: EV064374875US
DATE: March 28, 2002

JC02 Rec'd PCT/PTO 28 MAR 2002

FORM PTO 1390 (REV 11-2000) U S DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTORNEY'S DOCKET NUMBER
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371		REGIM-013
		US APPLICATION NO (If known, see 37 CFR 1 5) 10/089505
INTERNATIONAL APPLICATION NO. PCT/FR00/02773	INTERNATIONAL FILING DATES 5 October 2000	PRIORITY DATE CLAIMED 5 October 1999
TITLE OF INVENTION REACTOR FOR CULTURING CELLS OR MICRO-ORGANISMS OR FOR DISSOLVING OR SUSPENDING POWDER IN A LIQUID MEDIUM		
APPLICANT(S) FOR DO/EO/US Jean Rousseau and Jean-Pascal Zambaux		

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [x] This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing 35 U.S.C. 371
3. [x] This is an express request to begin national examination procedures (35 U.S.C. 371 (f)). The submission must include items (5), (6), (9) and (21) indicated below.
4. [x] The US has been elected by the expiration of 19 months from the priority date (PCT Article 31).
5. [x] A copy of the International Application as filed (35 U.S.C. 371 (c)(2))
   a. [ ] is attached hereto (required only if not communicated by the International Bureau).
   b. [x] has been communicated by the International Bureau.
   c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US).
6. [x] An English language translation of the International Application as filed (35 U.S.C. 371 (c)(2)).
   a. [x] is attached hereto.
   b [ ] has been previously submitted under 35 U.S.C. 154(d)(4)
7. [x] Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3))
   a. [ ] are attached hereto (required only if not communicated by the International Bureau).
   b. [ ] have been communicated by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [x] have not been made and will not be made.
8. [ ] An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).
9. [ ] An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).
10. [ ] An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C 371 (c)(5)).

Items 11 to 20 below concern document(s) or information included:

11 [ ] An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12 [ ] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. [ ] A FIRST preliminary amendment.
14. [ ] A SECOND or SUBSEQUENT preliminary amendment
15. [ ] A substitute specification.
16. [ ] A change of power of attorney and/or address letter.
17 [ ] A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 - 1.825.
18. [x] A second copy of the published international application under 35 U.S.C. 154(d)(4)
19. [ ] A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
20. [x] Other items or information: Copy of International Preliminary Examination Report (French & English), Copy of International Search Report (French & English), Two (2) Sheets of Formal Drawings, Application Data Sheet

JC13 Rec'd PCT/PTO 28 MAR 2002

U.S. APPLICATION NO (if known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO	ATTORNEY'S DOCKET NUMBER
10/089505	PCT/FR00/02773	REGIM-013

21. [x] The following fees are submitted:

BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) – (5)):

		CALCULATIONS PTO USE ONLY
[ ]	Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO . . $1040.00	
[x]	International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO . $890.00	
[ ]	International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO $740.00	
[ ]	International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) $710.00	
[ ]	International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) $100.00	
	ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 890.00
	Surcharge of $____ for furnishing the oath or declaration later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492 (e)).	$

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	
Total claims	17-20 =		x	$ 0.00
Independent claims	1-3 =		x	$ 0.00
MULTIPLE DEPENDENT CLAIM(s) (if applicable)			+ 280.00	$ 280.00
			TOTAL OF ABOVE CALCULATIONS =	$ 1,170.00
[x] Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by ½.				$ 585.00
			SUBTOTAL =	$ 585.00
Processing fee of $____ for furnishing the English translation later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492 (f)). +				$
			TOTAL NATIONAL FEE =	$ 585.00
Fee for recording the enclosed assignment (37 CFR 1.21 (h)). Assignment must be accompanied by appropriate cover sheet (37 CFR 3.28, 3.31) + (per property).				$
			TOTAL FEES ENCLOSED =	$ 585.00
			Amount to be Refunded:	$
			Charged:	$

a. [ ] A check in the amount of $____ to cover the above fees is enclosed.

b. [x] Please charge my Deposit Account No. 12-1095 in the amount of $ 585.00 to cover the above fees A duplicate copy of this sheet is enclosed.

c. [x] The Commissioner is hereby authorized to charge any additional fees which may be required or credit any overpayment to my Deposit Account No. 12-1095 . A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO.

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32,137

REGISTRATION NUMBER

2/prts

Reactor for culturing cells or microorganisms or for dissolving or suspending a powder in a liquid medium

The present invention relates to a reactor for culturing cells or microorganisms, or for dissolving or suspending a powder in a liquid medium.

One particularly advantageous application of the invention is in the field of biotechnology, and more particularly in the field of the pharmaceutical industry in which cell cultures and cultures of microorganisms are regularly used as a means of producing therapeutic molecules.

One particularly advantageous application of the invention is also in the field of pharmacy for the manufacture of medicaments or else in the agri-foodstuff and cosmetic fields.

Cultures of microorganisms such as bacteria, fungi and yeasts are normally produced in bioreactors of large volume allowing mass production on an industrial scale.

Plant cell cultures are produced instead in apparatuses of small volume and still remain at the present time at the development stage since the production cost hinders their extension.

The culturing of animal and human cells constitutes at the present time one of the major thrusts in the pharmaceutical industry, as they allow new therapeutic approaches, such as gene therapy, to be implemented.

This is because these cell cultures are used either as the actual essence of the medicament within the context of cell therapy or as a means of producing viral vectors used in gene therapy.

Cell therapy consists in removing certain cell populations from a patient so as to cultivate them and reinject them so as to reestablish or accentuate a particular activity.

As regards gene therapy, this has the objective of restoring, in the tissues of a patient, a deficient biological function by introducing therapeutic genes by means of appropriate viral vectors.

At the present time, cell cultures and cultures of microorganisms are produced in reactors having volumes varying between 1 and 5000 liters.

The reactors known at the present time comprise a glass or stainless steel tank, glass being used more for the small volumes and stainless steel for the larger volumes. They also include a propeller stirrer mounted in the bottom of the tank in order to stir the culture medium and keep the cells in continuous suspension.

Oxygenation of the culture medium in these known reactors preferably takes place with air, or else with pure oxygen, which is more difficult to regulate and which has the risk of oxidizing the culture medium. Oxygenation may also be carried out with air enriched with 30% oxygen.

After each culturing of cells or microorganisms, these reactors must be washed, decontaminated and rinsed. They are sterilized before each new culturing, either in an autoclave in the case of small-volume reactors or by injecting steam in the case of larger-volume reactors.

The operations of washing, maintaining and sterilizing these reactors are steps which are lengthy but essential for their operation.

In terms of cost, time and human resources, they may represent up to 30% of the operation of the reactor, which is very high.

Compared with the aforementioned prior art, the invention provides a novel reactor for culturing cells or microorganisms, which is simple, easy to use and of relatively low manufacturing cost and which is disposable.

More particularly, the invention provides a disposable reactor which comprises an outer envelope and at least one inner envelope which are made of plastic, these being placed in one another so as to define, on the one hand, inside said inner envelope, an inner compartment and, on the other hand, between the inner and outer envelopes, at least one outer compartment, said compartments being intended to contain a liquid medium, said envelopes being closed in a sealed manner with respect to the external environment and communicating with one another, which reactor is provided with means for injecting a pressurized gas into said inner compartment and means for removing said gas from said outer compartment in order to stir the liquid medium by making it flow between said compartments.

The liquid medium is advantageously a culture medium.

Thus, according to the invention, this single-use reactor allows the user to dispense with any washing and maintenance operation, this representing a very substantial saving in terms of time and money.

According to an advantageous characteristic of the reactor according to the invention, each inner envelope has an opening in its bottom and at least two lateral openings capable of establishing communication between

the inner and outer compartments, the opening provided in the bottom of said inner envelope having a much greater cross section than those of said lateral openings.

The diameter of the lateral openings is determined so that said openings can allow the culture medium to pass through them at a rate sufficient to break the ascending flux of the medium between the two envelopes, while said medium is being stirred.

The diameter of the opening at the bottom is determined so that the opening is large enough for the liquid flux to pass mainly through said opening and for the particles of the culture medium to be completely resuspended.

According to other nonlimiting and advantageous features of the reactor according to the invention:

- it includes means for injecting gas into the inner compartment. The gas is advantageously pure oxygen for oxygenating the culture medium, or nitrogen in order to prevent oxygenation of the medium;
- each inner envelope has a band of perforations extending approximately transversely to the longitudinal direction of said envelope, said perforations favoring transfer of the gas from one compartment to the other;
- the gas injection means comprise a plastic nozzle connected in a sealed manner to said inner envelope so that one of its ends emerges in the inner compartment, the other end emerging outside said reactor;
- said gas injection and discharge means comprise plastic nozzles connected in a sealed manner to said inner and outer envelopes respectively, so that one of their ends emerges in one of said inner and outer compartments, the other end emerging outside the

reactor;

- each gas inlet and outlet is provided with an absolute filter so as to avoid any possible contamination by contaminating agents conveyed by said gas from the liquid medium contained in said envelopes of the reactor;

- the outer envelope of the reactor has, laterally, at least one tap-off for introducing the culture medium into said compartments;

- said inner and outer envelopes are made of a flexible material, preferably a flexible polyvinyl chloride film, or a polyurethane film; and

- the reactor includes a sampling bag made of a flexible plastic material and connected in a sealed manner to said outer envelope so that it communicates with the outer compartment in order that, with the liquid medium being stirred, part of the latter is poured out into said sampling bag.

The description which follows, in conjunction with the appended drawings, given by way of nonlimiting examples, will make what the invention consists of and how it may be realized more clearly understood.

In the appended drawings:

- figure 1 shows a front view of a preferred embodiment of the reactor according to the invention; and

- figure 2 is a table of values of volumes of the reactor according to the invention.

Figure 1 shows a disposable reactor 100 for culturing cells or microorganisms.

Of course, this reactor may be designed to be used for suspending or dissolving solid particles in a liquid medium.

This reactor 100 comprises an outer envelope 101 and an inner envelope 102 which are made of a flexible plastic and placed in one another so as to define, on the one hand, inside said inner envelope 102, an inner compartment and, on the other hand, between the inner envelope 102 and outer envelope 101, an outer compartment.

The inner envelope 102 and outer envelope 101 constitute flexible bags, one inserted inside the other.

The reactor 100 has here a useful volume of about 20 liters, which represents an outer envelope 101 with a width of 360 mm and an inner envelope 102 with a width of about 260 mm.

The two, inner and outer, envelopes 101, 102 are positioned with respect to each other so as to be concentric with respect to a longitudinal axis X.

Of course, reactors of the same type could be provided which have a larger volume, ranging up to at least 400 - 500 liters.

Said envelopes 101, 102 are preferably made of a flexible polyvinyl chloride film which is high-frequency weldable, inexpensive and has good mechanical strength.

Provision may also be made for the outer and inner envelopes to be made of polyurethane, which resists heat well and has great mechanical strength.

The inner envelope 102 and outer envelope 101 are closed in a sealed manner with respect to the external environment and communicate with each other.

The envelopes 101, 102 are sealed along their upper edges 101a, 102a preferably by high-frequency welding so that the weld joins them together.

The inner envelope 102 has an opening 104 in its bottom and at least two lateral openings 105 capable of establishing communication between the inner and outer compartments, the opening 104 provided in the bottom of said inner envelope having a much greater cross section than that of the lateral openings.

More particularly, the opening 104 provided in the bottom of the inner envelope 102 has here a width when flat of 60 mm. This width has been carefully determined so that the opening 104 is large enough for the flux of liquid culture medium to pass mainly through this opening and for the particles which have settled in the culture medium to be completely resuspended.

The diameter of the lateral openings 105 of the inner envelope 102 has been determined so that these lateral openings can allow a sufficient flow of liquid to pass through them so as to break the ascending flux of liquid medium between the two envelopes and prevent the flexible inner envelope 102 from being bent during the ascent of said liquid medium in the inner compartment, thereby making it possible to obtain good homogenization of said culture medium.

The liquid medium in the reactor 100 is stirred with the aid of means for injecting a pressurized gas into said inner compartment and with the aid of means for discharging said gas from said outer compartment so as to make the culture medium flow between said compartments via said openings 104, 105.

The term "pressurized gas" is understood here to mean a gas under a slight overpressure with respect to

atmospheric pressure (an overpressure of a few mbar is sufficient).

According to the example shown, the gas injection and discharge means comprise nozzles 103, 103' connected in a sealed manner to said inner envelope 102 and outer envelope 101 respectively, so that one of their ends emerges in one of said inner and outer compartments and the other end emerges outside the reactor.

The nozzles 103 are intended to be connected to a pressurized gas feed (not shown), preferably a pressurized air feed.

Thus, the stirring of the medium in the reactor according to the invention is based on fluid mechanics so as to make the culture medium perfectly homogeneous. The pressure exerted in the inner compartment of the reactor causes the culture medium to rise in the outer compartment defined between the two envelopes, the supernatant decanted matter therefore being immediately resuspended.

When the pressure is released, the level of the liquid medium returns to its initial state in the inner compartment, thereby also causing the medium to be stirred.

The leaktight connection between the plastic nozzles 103, 103' and said envelopes 102, 101 is made when the two envelopes are welded together.

The reactor 100 also includes means for injecting a gas, here pure oxygen, into the inner compartment in order to oxygenate the culture medium.

These pure oxygen injection means may comprise a plastic nozzle, independent of the nozzles 103, 103',

which is connected in a sealed manner to the inner envelope of the reactor so that one of its ends emerges in the inner compartment, the other end emerging outside the reactor, in order for it to be connected to a pure oxygen feed.

According to the embodiment shown, the pressurized gas is injected into the inner compartment simultaneously with the injection of pure oxygen via the same nozzles 103.

Advantageously, the inner envelope 102 of the reactor includes a band of perforations 106 extending approximately transversely to the longitudinal direction X of the envelope 102, said perforations 106 favoring the transfer of pure oxygen from one compartment to the other.

The density of the perforations is determined according to the intended degree of oxygenation of the culture medium contained in said envelopes. Furthermore, the thermoplastic used to produce the inner and outer envelopes of the reactor is permeable to the gas, and especially to oxygen, so as to increase the area for exchange between the culture medium and the environment and therefore to optimize the oxygenation of the medium.

The outer envelope 101 includes, laterally, a tap-off, here a sealed plug 107 allowing the culture medium to be introduced and extracted. This tap-off 107 is protected by a suitable adhesive tamper-evident tab and can be opened by perforating the outer envelope in a perfectly sterile manner.

As figure 1 shows, the reactor furthermore includes at least one plastic pipe 108 which is connected in a sealed manner to said outer envelope (in the same way

as the other nozzles) and emerges at one end in the bottom of the inner compartment and at another end outside the reactor, in order to introduce various measurement probes.

In particular, it is possible to introduce a pH probe or an oxygen probe to check whether sufficient oxygen has been transferred during culturing of the medium contained in the compartments of the reactor. This pipe is made of a thermoplastic and is welded to the inner and outer envelopes in a perfectly sealed manner, preferably by high-frequency welding.

The temperature in the rector 100 is advantageously regulated with the aid of a vortex tube which is connected in a sealed manner to the outer envelope and emerges at one end in the bottom of the outer compartment and at the other end outside the reactor. The vortex tube converts an ordinary compressed-air supply into two streams of air: one hot and the other cold, at a pressure slightly above atmospheric pressure. A throttling valve on the hot outlet .of the tube (not shown) makes it possible to adjust the flow rates and temperatures over a continuous range. This heating or cooling system is regulated by a temperature probe (not shown) slipped into the pipe 108.

Advantageously, the reactor 100 may include a sampling bag (not shown) made of a flexible thermoplastic and connected in a sealed manner by a weld to said outer envelope so that it communicates with the outer compartment. In this way, when the liquid medium is stirred, part of the latter is poured out into said sampling bag and samples may be taken at any moment, during the culturing of the medium, with the aid of a clip which heat-seals and cuts off a sample bag from the sampling bag in order to recover a defined amount of sample of the liquid medium. This allows sequenced

sampling to be carried out.

However, provision may be made for this reactor not to have such a sampling bag and for the medium to be recovered after culturing by opening the envelopes.

The reactor is drained with the aid of a pump (not shown) provided on the upstream side with a filter which may be connected to the nozzle 103' shown in figure 1. This pump is associated with a hollow dip tube (not shown) which makes it possible to sample the medium via the bottom of the reactor 100.

According to the example shown, the minimum height of the inner envelope 102 has been set at 260 mm and the maximum height of the liquid medium in said envelopes is set here at 900 mm.

The difference between the widths of the two envelopes 101, 102 was determined by trials so that the inner envelope is wide enough and allows a large area for exchange between the liquid medium and the air or oxygen.

The volume of the outer compartment, that is to say the space provided between the two envelopes, must be large enough to allow the liquid medium to be properly removed from the inner envelope and for the culture medium to be made perfectly homogeneous.

The range of volumes for this type of reactor 100 is between 11 and 20 liters, knowing that there is complete homogenization of the medium contained in the reactor, even a 20 liter reactor. The various volumes appear in table 1 shown in figure 2.

The reactor 100 is advantageously delivered ready for use, is perfectly sterile and is optionally fitted with

all the probes necessary for using it. It may be prefilled with the culture medium.

Furthermore, a rigid retaining tank may be provided, in which said outer and inner flexible envelopes are suspended with the aid of standard suspension means. This retaining tank is then perfectly sealed and ensures that the system is secure should the outer envelope be inopportunely pierced.

The present invention is in no way limited to the embodiment described and shown, rather a person skilled in the art will be able to make any variant thereof in accordance with its spirit.

In particular, provision may be made for the inner and outer envelopes to be made of a rigid plastic.

The reactor according to the invention may also be provided so as to comprise a number of envelopes greater than 2, these being imbricated in one another so as to define an inner compartment at the center of the reactor and a plurality of concentric outer compartments surrounding said inner compartment, all of the compartments communicating with one another in order for the culture medium to flow between said compartments.

CLAIMS

1. A disposable reactor (100) for culturing cells or microorganisms or for dissolving or suspending a powder in a liquid medium, which comprises an outer envelope (101) and at least one inner envelope (102) which are made of plastic, these being placed in one another so as to define, on the one hand, inside said inner envelope, an inner compartment and, on the other hand, between the inner and outer envelopes, at least one outer compartment, the compartments being intended to contain a liquid medium, said envelopes being closed in a sealed manner with respect to the external environment and communicating with one another, which reactor is provided with means for injecting a pressurized gas into said inner compartment and means for removing said gas from said outer compartment in order to stir the liquid medium by making it flow between said compartments.

2. The reactor (100) as claimed in claim 1, characterized in that each inner envelope has an opening (104) in its bottom and at least two lateral openings (105) capable of establishing communication between the inner and outer compartments, the opening provided in the bottom of said inner envelope having a much greater cross section than that of said lateral openings.

3. The reactor (100) as claimed in either of claims 1 and 2, characterized in that it includes means for injecting a gas such as pure oxygen or else nitrogen into the inner compartment.

4. The reactor (100) as claimed in claim 3, characterized in that each inner envelope has a band of perforations (106) extending approximately transversely to the longitudinal direction of said envelope, said

perforations favoring transfer of the gas from one compartment to the other.

5. The reactor (100) as claimed in either of claims 3 and 4, characterized in that said gas injection means comprise a plastic nozzle connected in a sealed manner to said inner envelope so that one of its ends emerges in the inner compartment, the other end emerging outside said reactor.

6. The reactor (100) as claimed in one of claims 1 to 5, characterized in that said gas injection and discharge means comprise plastic nozzles (103, 103') connected in a sealed manner to said inner and outer envelopes respectively, so that one of their ends emerges in one of said inner and outer compartments, the other end emerging outside said reactor.

7. The reactor (100) as claimed in claim 6, characterized in that the injection of pressurized gas and of pure oxygen into said inner compartment takes place via the same nozzle (103).

8. The reactor (100) as claimed in one of the preceding claims, characterized in that it includes at least one plastic pipe (108) which is connected in a sealed manner to said outer envelope and emerges at one end in the bottom of the outer compartment and at the other end outside the reactor, in order to introduce a measurement probe.

9. The reactor (100) as claimed in one of the preceding claims, characterized in that it includes at least one vortex tube which is connected in a sealed manner to said outer envelope and emerges at one end in the bottom of the outer compartment and at the other end outside the reactor, in order to regulate the temperature of the liquid medium.

10. The reactor (100) as claimed in one of the claims 5 to 9, characterized in that each gas inlet and outlet is provided with an absolute filter.

11. The reactor (100) as claimed in one of the preceding claims, characterized in that said outer envelope has, laterally, a tap-off (107) for introducing the culture medium into said compartments.

12. The reactor (100) as claimed in one of the preceding claims, characterized in that said outer and inner envelopes are made of a flexible material.

13. The reactor (100) as claimed in claim 12, characterized in that said envelopes are made of a flexible polyvinyl chloride film.

14. The reactor (100) as claimed in claim 12, characterized in that said envelopes are made of a polyurethane film.

15. The reactor (100) as claimed in one of the preceding claims, characterized in that it includes a sampling bag made of a flexible plastic material and connected in a sealed manner to said outer envelope so that it communicates with the outer compartment in order that, with the liquid medium being stirred, part of the latter is poured out into said sampling bag.

16. The reactor (100) as claimed in one of claims 12 to 15, characterized in that the inner and outer envelopes (102, 101) are suspended in a rigid retaining tank.

(12) DEMANDE INTERNATIONALE PUBLIÉE EN VERTU DU TRAITÉ DE COOPÉRATION EN MATIÈRE DE BREVETS (PCT)

(19) Organisation Mondiale de la Propriété Intellectuelle
Bureau international

(43) Date de la publication internationale
12 avril 2001 (12.04.2001)

PCT

(10) Numéro de publication internationale
WO 01/25394 A1

(51) Classification internationale des brevets[7]: C12M 1/00

(21) Numéro de la demande internationale:
PCT/FR00/02773

(22) Date de dépôt international: 5 octobre 2000 (05.10.2000)

(25) Langue de dépôt: français

(26) Langue de publication: français

(30) Données relatives à la priorité:
99/12392 5 octobre 1999 (05.10.1999) FR

(71) Déposant *(pour tous les États désignés sauf US)*: ETABLISSEMENT VERDOT MECANIQUE GENERALE [FR/FR]; 13, rue Lavoisier, Z.A. Beaumont Romagnat, F-63110 Beaumont (FR).

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(81) États désignés *(national)*: BR, CA, MG, US, ZA.

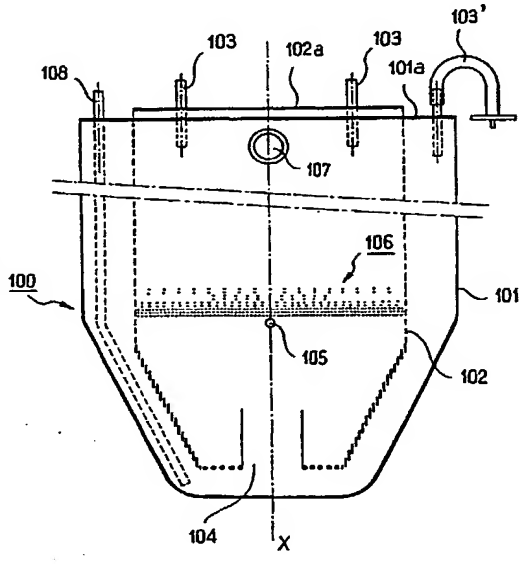
(84) États désignés *(régional)*: brevet européen (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Publiée:
— *Avec rapport de recherche internationale.*
— *Avant l'expiration du délai prévu pour la modification des revendications, sera republiée si des modifications sont reçues.*

En ce qui concerne les codes à deux lettres et autres abréviations, se référer aux "Notes explicatives relatives aux codes et abréviations" figurant au début de chaque numéro ordinaire de la Gazette du PCT.

(54) Title: REACTOR FOR CULTURING CELLS OR MICRO-ORGANISMS OR FOR DISSOLVING OR SUSPENDING POWDER IN A LIQUID MEDIUM

(54) Titre: REACTEUR POUR LA REALISATION DE CULTURES CELLULAIRES OU DE MICRO-ORGANISMES OU POUR LA MISE EN SOLUTION OU EN SUSPENSION DE POUDRE DANS UN MILIEU LIQUIDE



(57) Abstract: The invention concerns a disposable reactor (100) for culturing of cells or micro-organisms or for dissolving or suspending solid particles in a liquid medium, comprising an outer casing (101) and at least an inner casing (102) made of plastic material, nested into each other, said casings being tightly closed with respect to outside environment and communicating with each other, and it is provided with means supplying pressurised gas into said casings and means for evacuating said gas outside to stir the liquid medium contained in said casings by causing it to flow from one casing to the other.

(57) Abrégé: L'invention concerne un réacteur (100) jetable pour la réalisation de cultures de cellules ou de micro-organismes ou pour la mise en solution ou en suspension de particules solides dans un milieu liquide, qui comprend une enveloppe externe (101) et au moins une enveloppe interne (102) réalisées en matière plastique, placées l'une dans l'autre, lesdites enveloppes étant fermées de manière étanche vis-à-vis de l'environnement extérieur et communicant entre elles, et qui est pourvu de moyens d'arrivée d'un gaz sous pression dans lesdites enveloppes ainsi que de moyens d'évacuation dudit gaz vers l'extérieur pour agiter le milieu liquide contenu dans lesdites enveloppes en le faisant circuler d'une enveloppe à l'autre.

WO 01/25394 A1

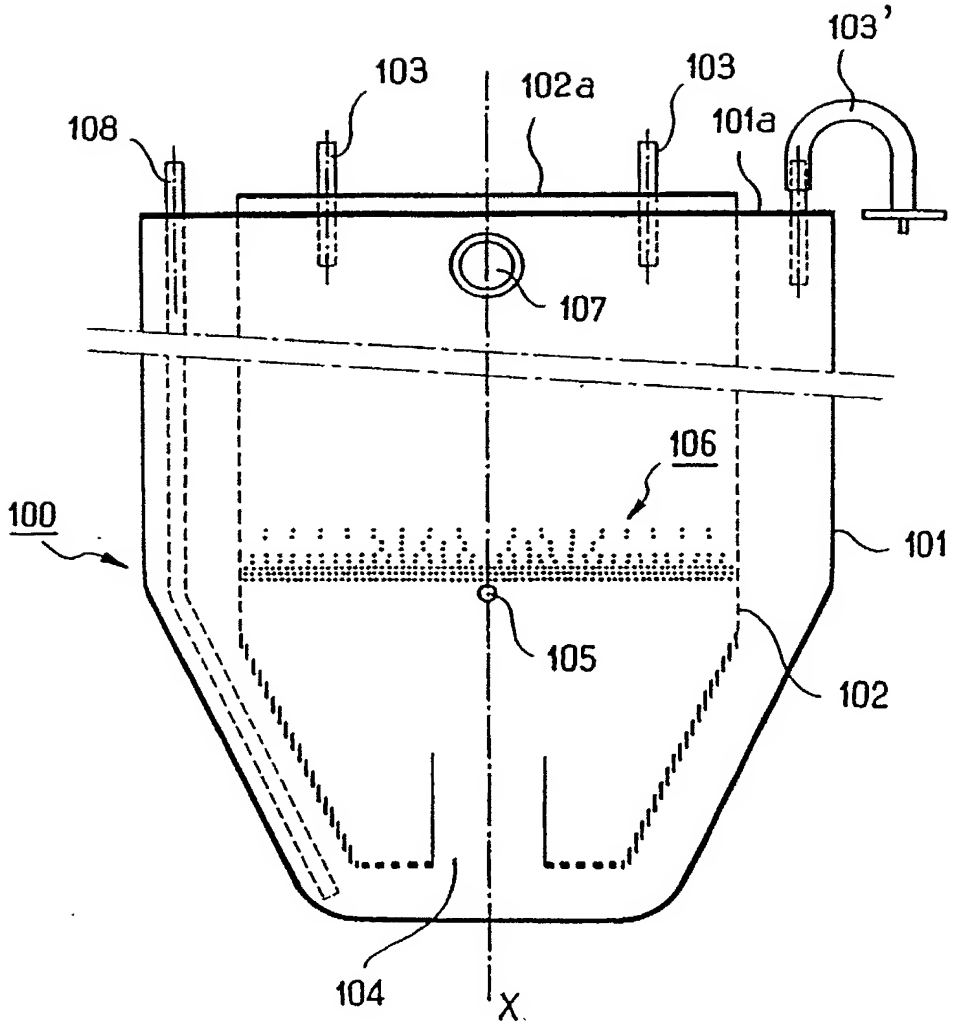


FIG_1

Internal R.	External R.	Min. water H. (mm)	~ inner	Displaced vol. (mm^3)	~ outer	Max. water H. (mm)	Min. water h (mm)	Water vol.
83	115	260	130	2797310	142	402	260	11
83	115	270	140	3012487	153	423	270	11
83	115	280	150	3227665	164	444	280	12
83	115	290	160	3442843	174	464	290	12
83	115	300	170	3658020	185	485	300	12
83	115	310	180	3873198	196	506	310	13
83	115	320	190	4088376	207	527	320	13
83	115	330	200	4303553	218	548	330	14
83	115	340	210	4518731	229	569	340	14
83	115	350	220	4733909	240	590	350	14
83	115	360	230	4949086	251	611	360	15
83	115	370	240	5164264	262	632	370	15
83	115	380	250	5379442	273	653	380	16
83	115	390	260	5594619	283	673	390	16
83	115	400	270	5809797	294	694	400	17
83	115	410	280	6024975	305	715	410	17
83	115	420	290	6240152	316	736	420	17
83	115	430	300	6455330	327	757	430	18
83	115	440	310	6670508	338	778	440	18
83	115	450	320	6885685	349	799	450	19
83	115	460	330	7100863	360	820	460	19
83	115	470	340	7316041	371	841	470	19
83	115	480	350	7531218	382	862	480	20
83	115	490	360	7746396	393	883	490	20

FIG_2

#4

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DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION (37 CFR 1.63)

[ ] Declaration Submitted with Initial Filing OR [X] Declaration Submitted after Initial Filing (surcharge (37 CFR 1.16 (e)) required)

Attorney Docket Number	REGIM-013
First Named Inventor	Jean Rousseau
COMPLETE IF KNOWN	
Application Number	UNKNOWN
Filing Date	
Group Art Unit	N/A
Examiner Name	Not Yet Assigned

As a below named inventor, I hereby declare that:

My residence, mailing address, and citizenship are as stated below next to my name.

I believe I am the original and first inventor of the subject matter which is claimed and for which a patent is sought on the invention entitled:

REACTOR FOR CULTURING CELLS OR MICRO-ORGANISMS OR FOR DISSOLVING OR SUSPENDING POWDER IN A LIQUID MEDIUM

(Title of the Invention)

the specification of which

[ ] is attached hereto

OR

[X] was filed on (MM/DD/YYYY) 10/05/2000 as United States Application Number or PCT International Application No. PCT/FR00/02773 and was amended on (MM/DD/YYYY) [ ] (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56, including for continuation-in-part applications, material information which became available between the filing date of the prior application and the national or PCT international filing date of the continuation-in-part application.

I hereby claim foreign priority benefits under 35 U.S.C. 119(a)-(d) or (f), or 365(b) of any foreign application(s) for patent, inventor's or plant breeder's rights certificate(s), or 365 (a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent, inventor's or plant breeder's rights certificate(s), or of any PCT international application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application Number(s)	Country	Foreign Filing Date (MM/DD/YYYY)	Priority Not Claimed	Certified Copy Attached? YES	NO
99/12392	FR	10/05/1999	[ ]	[X]	[ ]
			[ ]	[ ]	[ ]
			[ ]	[ ]	[ ]
			[ ]	[ ]	[ ]

[ ] Additional foreign application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto:

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DECLARATION — Utility or Design Patent Application

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following registered practitioner(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith: Customer Number 000530

Direct all correspondence to [X] Customer Number or Bar Code Label 000530 OR [ ] Correspondence address below

Name

Address

City | State | ZIP

Country | Telephone | Fax

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

NAME OF SOLE OR FIRST INVENTOR: [ ] A petition has been filed for this unsigned inventor

Given Name (first and middle [if any]): 1-00 Jean | Family Name or Surname: Rousseau

Inventor's Signature | Date: July 30, 2002

Residence: City: Auxonne | State | Country: France | Citizenship: France FRX

Mailing Address: Villers Rotin

City: Auxonne | State | ZIP: F-21110 | Country: France

NAME OF SECOND INVENTOR: [ ] A petition has been filed for this unsigned inventor

Given Name (first and middle [if any]): 2-00 Jean-Pascal | Family Name or Surname: Zambaux

Inventor's Signature | Date: July 30, 2002

Residence: City: Annecy | State | Country: France | Citizenship: France FRX

Mailing Address: 95, route du Périmètre

City: Annecy | State | ZIP: F-74000 | Country: France

[ ] Additional inventors are being named on the ____ supplemental Additional Inventor(s) sheet(s) PTO/SB/02A attached hereto.